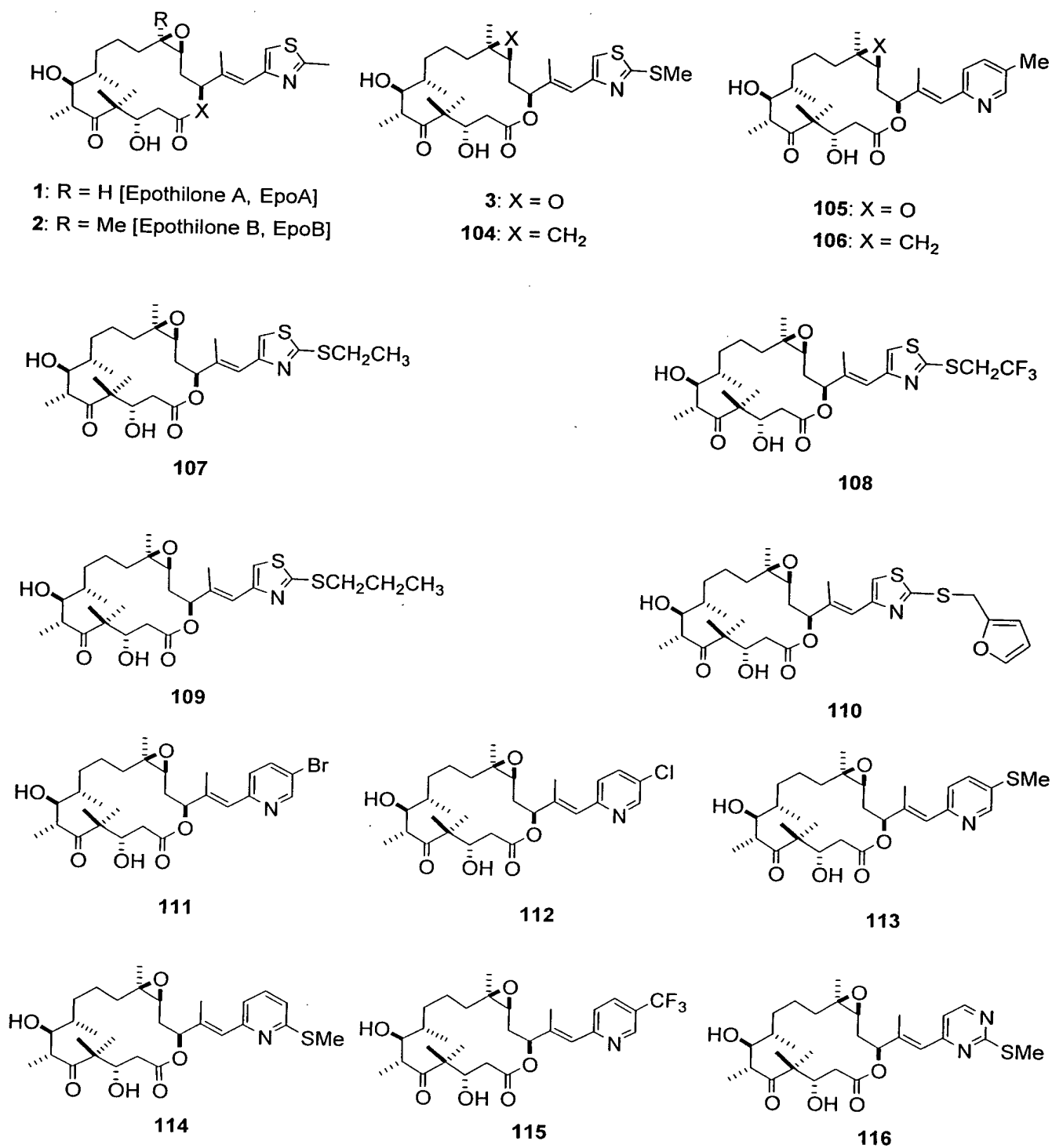
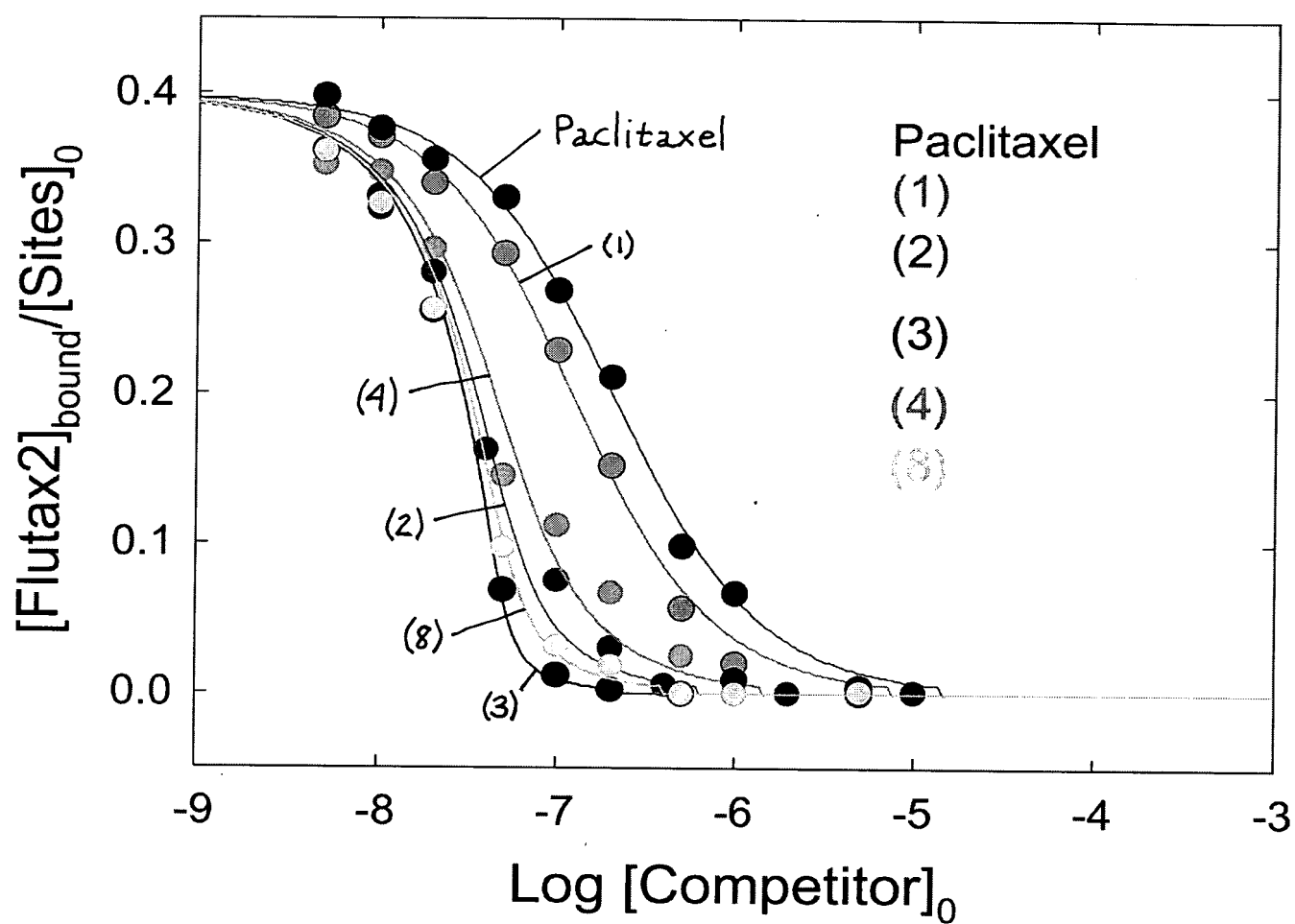


Figure 1A



**Figure 1B**



**FIGURE 2**

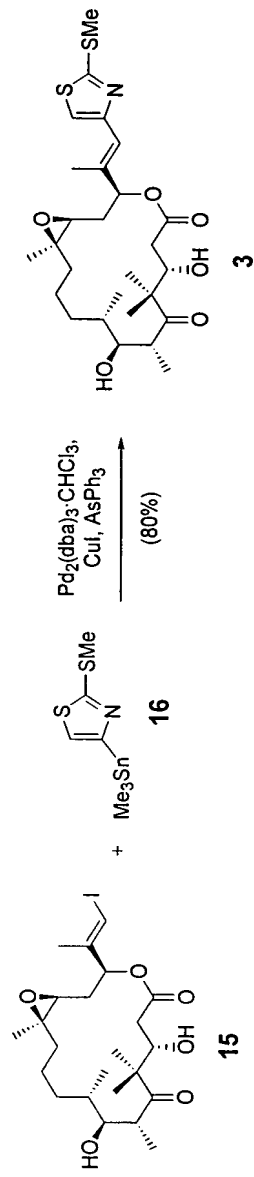
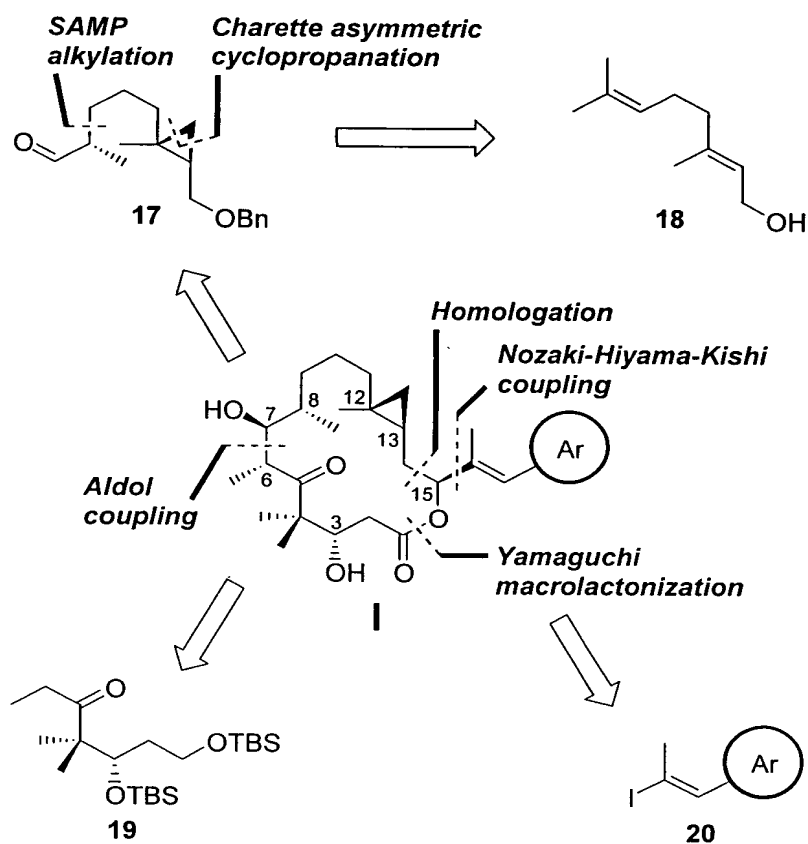


Figure 3



**Figure 4**

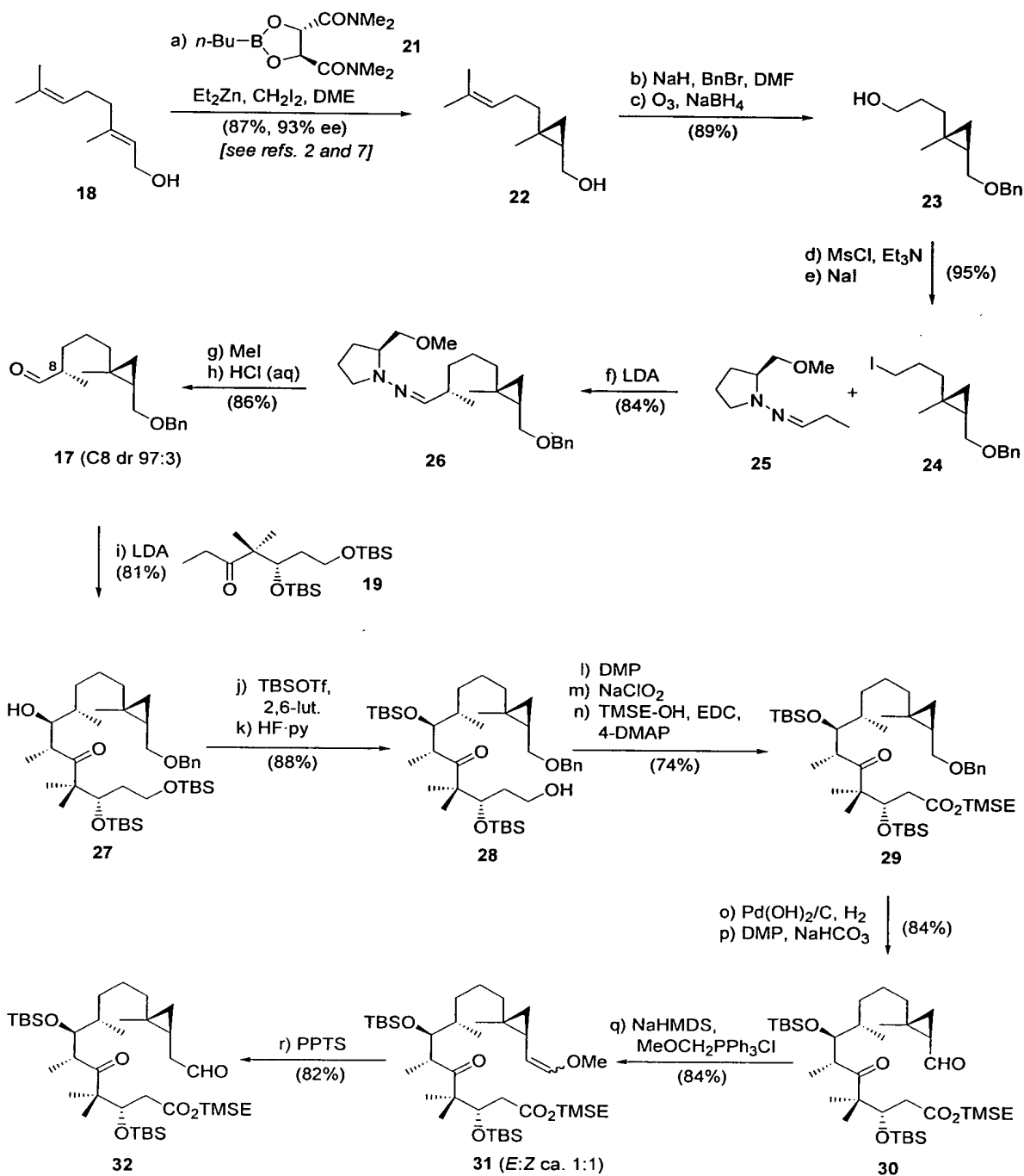
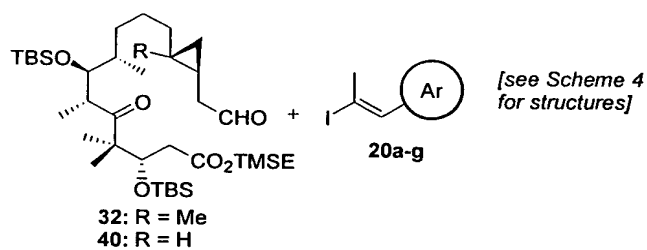
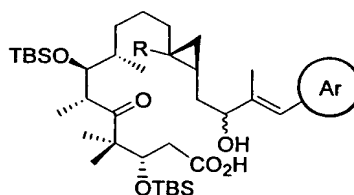


Figure 5



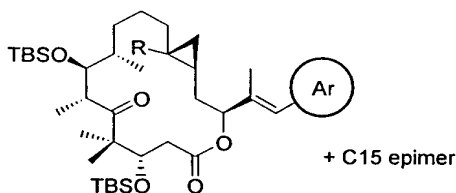


a)  $\text{CrCl}_2$ ,  $\text{NiCl}_2$ , 4-*t*-Bu-py  
 b) TBAF



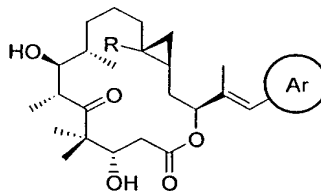
Entry	1	2	3	4	5	6	7	8
Compound	41a	41b	41d	41e	41f	41g	42c	42e
R	Me	Me	Me	Me	Me	Me	H	H
Yield (%)	73	57	49	62	63	46	46	39

c)  $\text{Et}_3\text{N}$ , 2,4,6-trichlorobenzoyl-chloride, 4-DMAP



Entry	1	2	3	4	5	6	7	8
Compound	43a	43b	43d	43e	43f	43g	44c	44e
R	Me	Me	Me	Me	Me	Me	H	H
Yield (%)	33	28	35	35 <sup>g</sup>	35	37	33	47

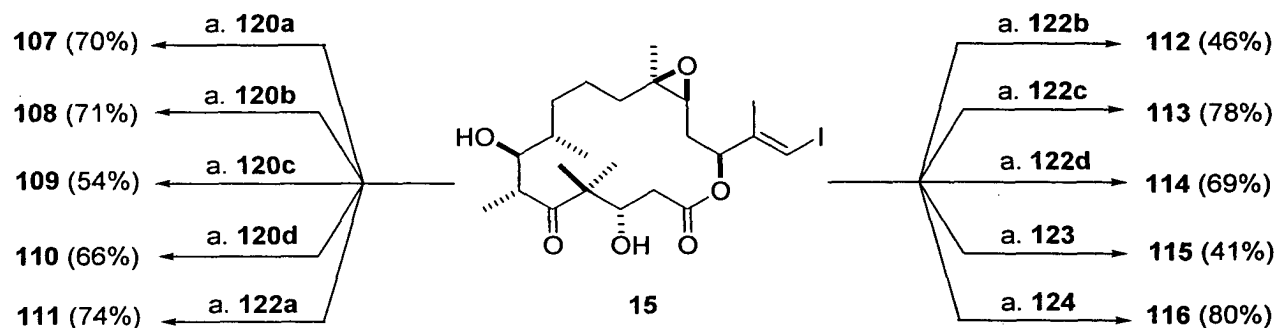
d) 20% TFA in  $\text{CH}_2\text{Cl}_2$



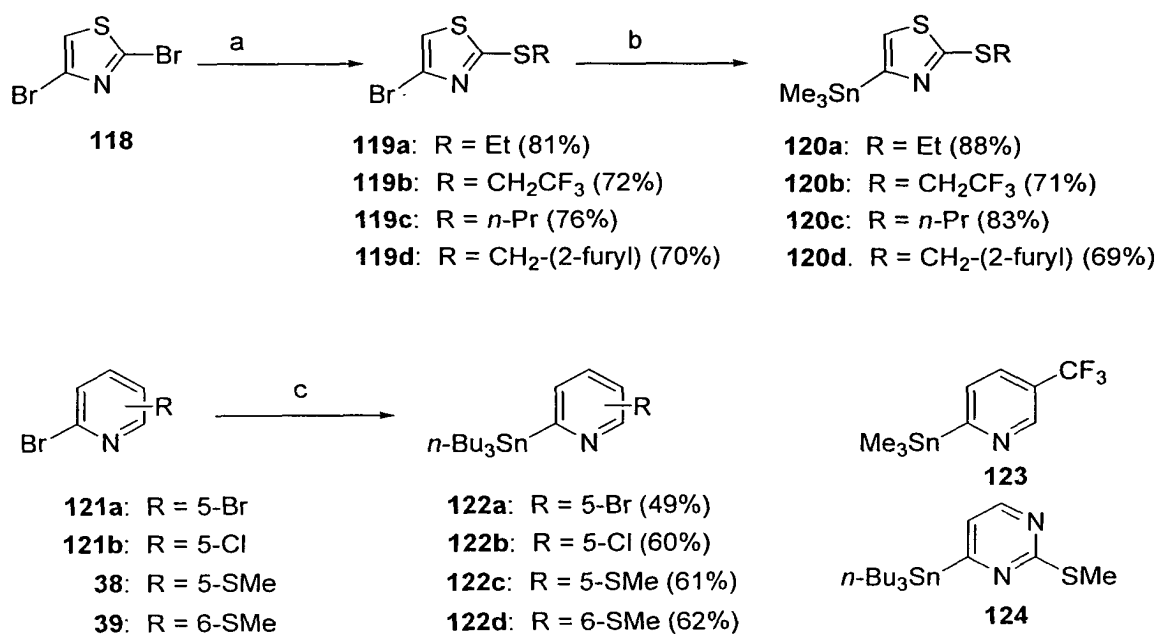
Entry	1	2	3	4	5	6	7	8
Compound	6	8	10	12	13	14	9	11
R	Me	Me	Me	Me	Me	Me	H	H
Yield (%)	73	48	56	49	68	48	54	68

Figure 7

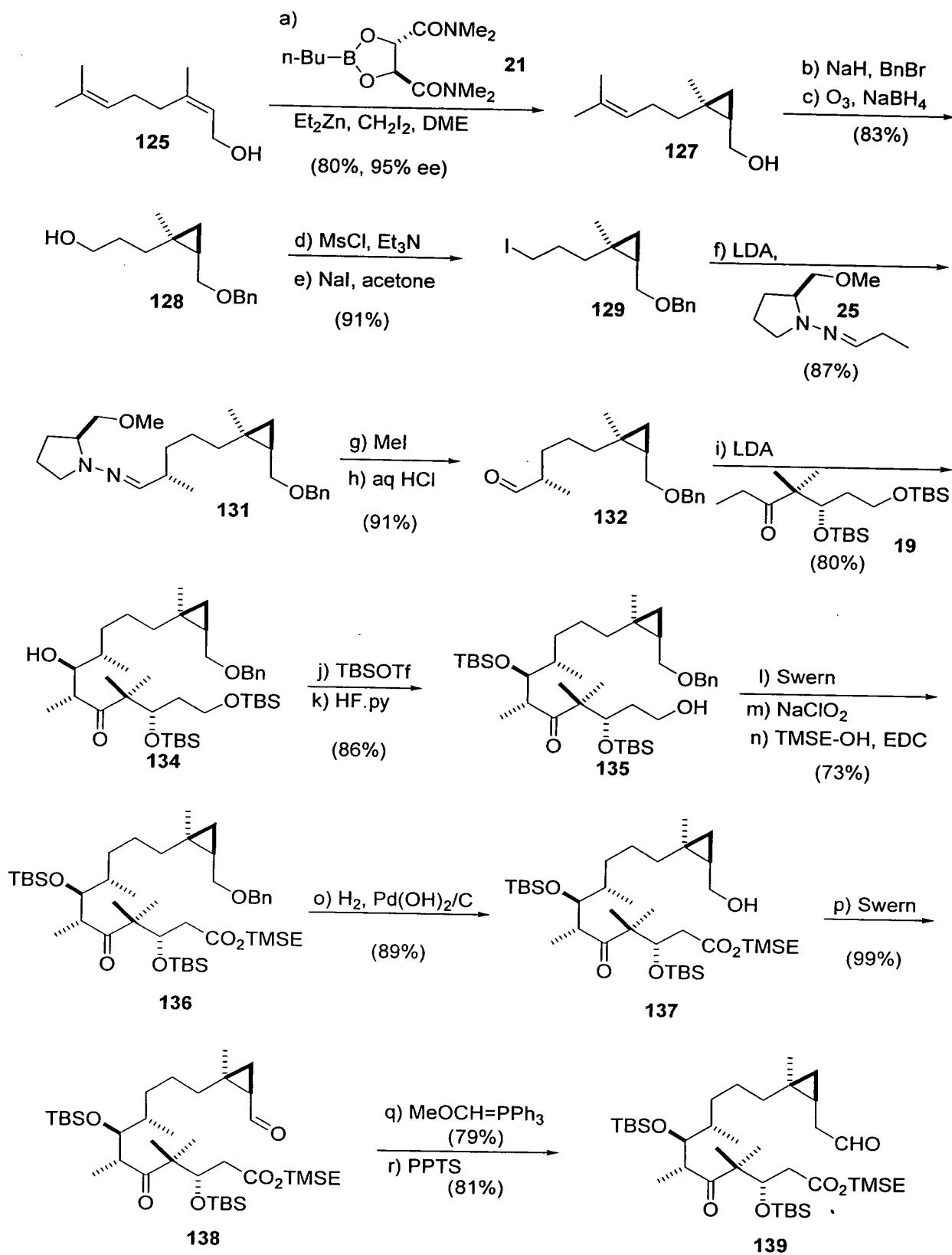




**Figure 8**



**Figure 9**



**Figure 10**

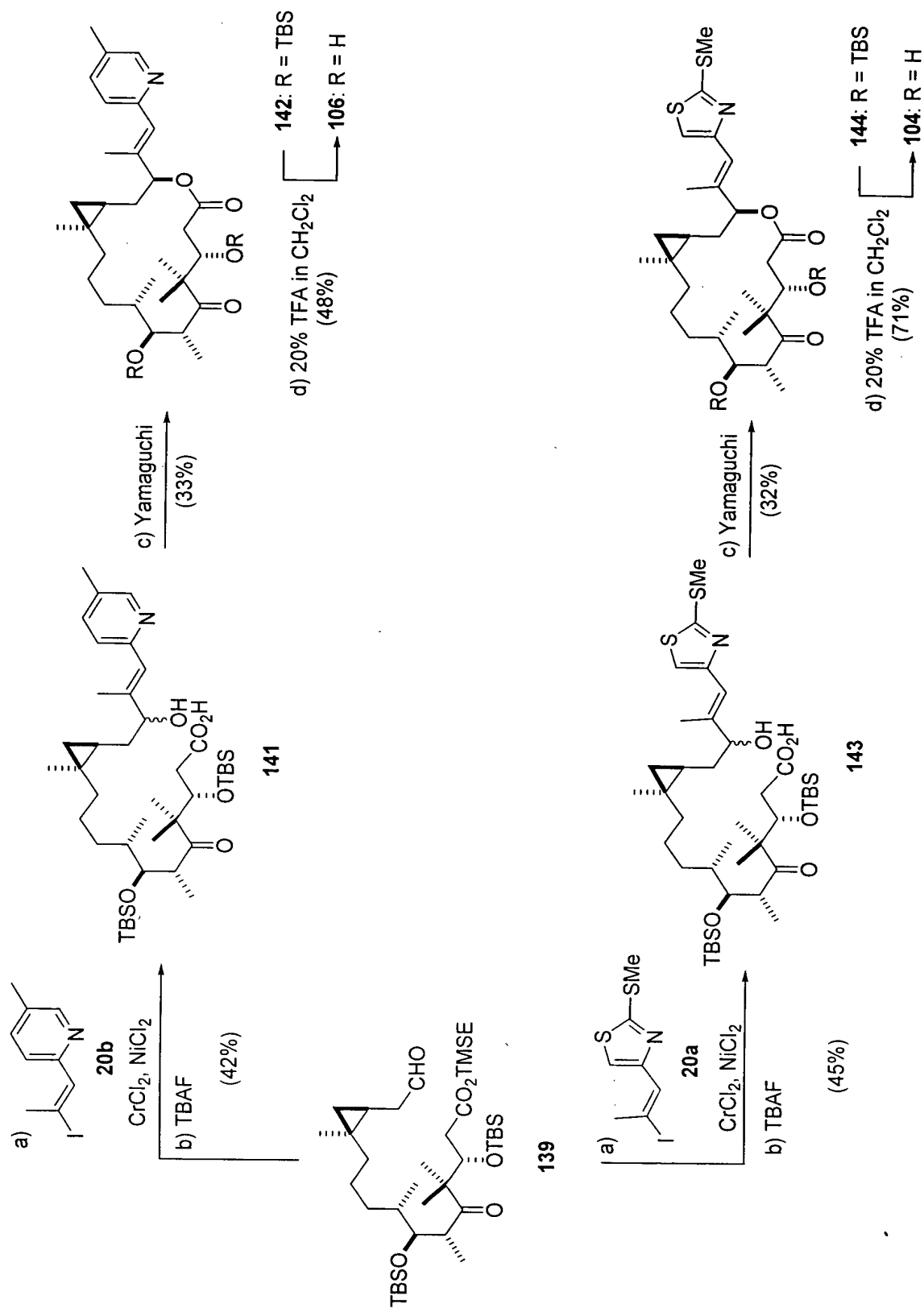


Figure 11

Compound	Cell Line					
	1A9		A8		PTX10	
	IC <sub>50</sub> (nM)	RR	IC <sub>50</sub> (nM)	RR	IC <sub>50</sub> (nM)	RR
Taxol <sup>TM</sup>	3.0 ± 0.4	3.3	10.1 ± 2.9	3.3	89.7 ± 9.0	29.5
Epo A	2.4 ± 0.6	38.7	91.0 ± 10.0	38.7	34.2 ± 2.0	14.5
Epo B	0.6 ± 0.3	10.7	6.5 ± 0.9	10.7	3.1 ± 0.5	5.2
3	0.17 ± 0.8	7.6	1.3 ± 0.65	7.6	0.26 ± 0.11	1.5
104	0.1 ± 0.0	23.5	2.4 ± 1.1	23.5	0.7 ± 0.3	6.5
106	0.3 ± 0.1	41.4	10.4 ± 2.4	41.4	3.3 ± 1.2	13.2
108	3.5 ± 0.7	5.3	18.4 ± 1.4	5.3	16.1 ± 2.1	4.6
109	4.4 ± 2.4	9.7	42.9 ± 5.1	9.7	24.7 ± 4.9	5.6
110	2.1 ± 0.8	7.6	16.0 ± 5.5	7.6	9.8 ± 1.4	4.7
111	0.7 ± 0.2	16.6	11.1 ± 1.0	16.6	3.9 ± 0.4	5.8
112	3.2 ± 0.1	10.0	31.9 ± 3.1	10.0	16.1 ± 4.1	5.1
113	0.4 ± 0.1	31.7	11.6 ± 6.7	31.7	3.9 ± 1.1	10.5
114	3.3 ± 0.2	8.3	27.7 ± 3.2	8.3	12.2 ± 7.4	3.7
115	4.3 ± 0.4	19.2	83.0 ± 2.0	19.2	65.3 ± 11.9	15.1
116	8.6 ± 1.2	3.8	32.3 ± 2.7	3.8	42.9 ± 10.3	5.0
					IC <sub>50</sub> (nM)	RR
					53.4 ± 26.5	17.6
					8.7 ± 2.2	3.7
					0.8 ± 0.5	1.3
					0.25 ± 0.17	1.5
					0.6 ± 0.5	5.9
					1.3 ± 1.1	5.3
					3.8 ± 0.3	1.1
					5.2 ± 0.8	1.2
					2.9 ± 1.3	1.4
					0.3 ± 0.1	0.5
					3.2 ± 0.3	1.0
					2.1 ± 1.9	5.8
					6.6 ± 2.6	2.0
					9.6 ± 1.3	2.2
					9.6 ± 1.0	1.1

Figure 12

Compound	Cell Line	KB-31	KB-8511
		IC <sub>50</sub> (nM)	IC <sub>50</sub> (nM)
Epo B		0.19	0.12
3		0.11	0.07
104		0.20	0.12
106		0.44	0.29
108		3.04	2.67
109		10.0	6.73
110		1.16	1.28
111		0.72	0.55
113		0.54	0.41
114		4.87	3.24
115		8.38	7.37
116		9.01	11.65

**Figure 13**

**Figur 14**

Compound	Cell line						
	1A9	A8 (β274)		PTX10 (β270)		PTX22 (β364)	
	IC <sub>50</sub>	IC <sub>50</sub>	RR	IC <sub>50</sub>	RR	IC <sub>50</sub>	RR
epothilone A (Epo A) 1	3.1 ± 0.72	77.3 ± 9.25	24.9	29.1 ± 7.24	9.4	10.1 ± 2.10	3.3
epothilone B (Epo B) 2	0.3 ± 0.05	6.5 ± 1.70	21.7	3.7 ± 1.83	12.3	2.1 ± 1.45	7
paclitaxel (Taxol®)	1.3 ± 0.22	11.3 ± 0.83	8.7	47.7 ± 5.01	36.7	29.4 ± 3.69	22.6
tmt-epo B 3	0.17 ± 0.08	1.3 ± 0.65	7.6	0.26 ± 0.11	1.5	0.25 ± 0.17	1.5
cis-CP-py-epo A 4	2.4 ± 0.99	41.6 ± 8.58	17.3	19.2 ± 9.39	8	4.2 ± 2.18	1.8
trans-CP-epo A 5	10.1 ± 6.59	33.9 ± 5.56	3.4	17.2 ± 5.97	1.7	4.7 ± 1.68	0.5
trans-CP-epo B 6	15	>150	>10	52	3.5	5	0.3
trans-CP-py-epo A 7	0.6 ± 0.22	10.1 ± 2.07	16.8	5.9 ± 1.96	9.8	1.4 ± 0.51	2.3
trans-CP-py-epo B 8	1.7 ± 0.76	27.9 ± 6.73	16.4	10.9 ± 3.52	6.4	5.6 ± 3.24	3.3
trans-CP-pyOH-epo A 9	0.7 ± 0.16	13.0 ± 2.17	18.6	6.1 ± 1.90	8.7	1.1 ± 0.38	1.6
trans-CP-pyOH-epo B 10	1.7 ± 1.12	13.2 ± 5.02	7.8	10.2 ± 3.75	6	2.5 ± 1.41	1.5
trans-CP-tmt-epo A 11	1.2 ± 0.67	11.2 ± 2.30	9.3	3.2 ± 1.13	2.7	0.8 ± 0.38	0.7
trans-CP-tmt-epo B 12	3.5 ± 1.64	28.9 ± 8.01	8.3	5.7 ± 1.96	1.6	11.5 ± 3.86	3.3
trans-CP-5tmpy-epo B 13	14.2 ± 5.73	94 ± 5	6.6	72.0 ± 10.41	5.1	20.6 ± 9.06	1.5
trans-CP-6tmpy-epo B 14	114	>150	>1.3	>150	>1.3	104	0.9

**Figure 15**

Compound	% TP <sup>a</sup>	KB-31 <sup>b</sup>	KB-8511 <sup>b</sup>	RR
epothilone A (Epo A) <b>1</b>	78	2.15 <sup>c</sup>	1.91 <sup>c</sup>	0.88 <sup>c</sup>
epothilone B (Epo B) <b>2</b>	93	0.19 <sup>c</sup>	0.18 <sup>c</sup>	0.95 <sup>c</sup>
paclitaxel (Taxol®)	52	2.92 <sup>c</sup>	626 <sup>c</sup>	214 <sup>c</sup>
Tmt-epo B <b>3</b>	99	0.11	0.07	0.61
<i>cis</i> -CP-py-epo A <b>4</b>	100 <sup>c</sup>	0.62 <sup>c</sup>	0.45 <sup>c</sup>	0.72 <sup>c</sup>
<i>trans</i> -CP-epo A <b>5</b>	100 <sup>c</sup>	0.97 <sup>c</sup>	0.64	0.66 <sup>c</sup>
<i>trans</i> -CP-epo B <b>6</b>	82	1.84	1.09	0.59
<i>trans</i> -CP-py-epo A <b>7</b>	94 <sup>c</sup>	0.84 <sup>c</sup>	0.68 <sup>c</sup>	0.81 <sup>c</sup>
<i>trans</i> -CP-py-epo B <b>8</b>	89	0.90	0.61	0.68
<i>trans</i> -CP-pyOH-epo B <b>10</b>	87	0.44	0.55	1.25
<i>trans</i> -CP-tmt-epo A <b>11</b>	93	0.66	0.32	0.48
<i>trans</i> -CP-tmt-epo B <b>12</b>	91	0.67	0.45	0.67
<i>trans</i> -CP-5tmpy-epo B <b>13</b>	88	6.88	5.28	0.77
<i>trans</i> -CP-6tmpy-epo B <b>14</b>	58	109	74	0.68

**Figur 16**

Compound	$K_d$ (37 °C) <sup>b</sup>	$\Delta G_{app}^0$ (37 °C) <sup>c</sup>
epothilone A (Epo A) <b>1</b>	34 ± 4	-44.5 ± 0.3
epothilone B (Epo B) <b>2</b>	1.6 ± 0.1	-52.6 ± 0.5
paclitaxel (Taxol <sup>®</sup> )	93 ± 26	-42.2 ± 0.2
tmt-epo B <b>3</b>	0.64 ± 0.24	-54.5 ± 1.2
<i>cis</i> -CP-py-epo A <b>4</b>	5.2 ± 0.8	-49.4 ± 0.3
<i>trans</i> -CP-epo A <b>5</b>	6.5 ± 0.1	-48.6 ± 0.1
<i>trans</i> -CP-epo B <b>6</b>	8.0 ± 1.8	-48.0 ± 0.1
<i>trans</i> -CP-py-epo A <b>7</b>	2.1 ± 0.4	-51.5 ± 0.2
<i>trans</i> -CP-py-epo B <b>8</b>	1.9 ± 0.6	-51.8 ± 0.8
<i>trans</i> -CP-pyOH-epo B <b>10</b>	6.0 ± 0.6	-48.9 ± 0.3
<i>trans</i> -CP-tmt-epo A <b>11</b>	1.6 ± 0.5	-52.2 ± 0.9
<i>trans</i> -CP-tmt-epo B <b>12</b>	1.8 ± 0.2	-51.8 ± 0.3
<i>trans</i> -CP-5tmpy-epo B <b>13</b>	1.9 ± 0.3	-51.6 ± 0.5
<i>trans</i> -CP-6tmpy-epo B <b>14</b>	53 ± 8	-43.1 ± 0.5